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L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:1359036 CAPLUS

DOCUMENT NUMBER: 149:556830

TITLE: A new and efficient process for the preparation of cabergoline and its intermediates
 Li, Yuanqiang; Wang, Zhi-Xian; Kondamreddy, Murali; Cai, Xiongwei

INVENTOR(S):
 Li, Yuanqiang; Wang, Zhi-Xian; Kondamreddy, Murali; Cai, Xiongwei

PATENT ASSIGNEE(S): Apotex Pharmachem Inc., Can.

SOURCE: Can. Pat. Appl., 35pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

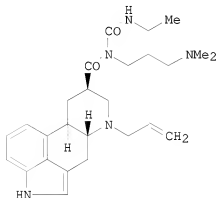
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2587880	A1	20081104	CA 2007-2587880	20070504
PRIORITY APPLN. INFO.:			CA 2007-2587880	20070504
OTHER SOURCE(S):			CASREACT 149:556830; MARPAT 149:556830	

GI



AB This invention relates to a new and efficient process for the production of dopamine agonists such as cabergoline (I) and the intermediates thereof.

IT 1075250-76-8P

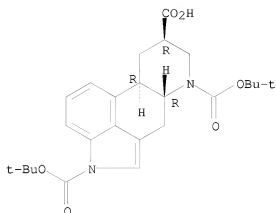
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for the preparation of cabergoline, an ergoline alkaloid with therapeutic usefulness as a dopamine receptor agonist)

RN 1075250-76-8 CAPLUS

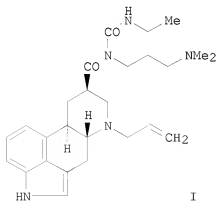
CN Ergoline-1,6,8-tricarboxylic acid, 1,6-bis(1,1-dimethylethyl) ester, (8β)- (CA INDEX NAME)

Absolute stereochemistry.

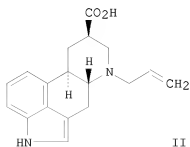


L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN
 ACCESSION NUMBER: 2008:1339686 CAPLUS
 DOCUMENT NUMBER: 149:534450
 TITLE: New and efficient process for the preparation of cabergoline and its intermediates
 INVENTOR(S): Wang, Zhi-Xian; Li, Yuanqiang; Kondamreddy, Murali; Cai, Xiongwei
 PATENT ASSIGNEE(S): Apotex Pharmachem Inc., Can.
 SOURCE: U.S. Pat. Appl. Publ., 19pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080275240	A1	20081106	US 2007-797510	20070504
PRIORITY APPLN. INFO.:			US 2007-797510	20070504
ASSIGNMENT HISTORY FOR	US PATENT AVAILABLE IN LSUS DISPLAY FORMAT			
OTHER SOURCE(S):	CASREACT 149:534450; MARPAT 149:534450			
GI				



I



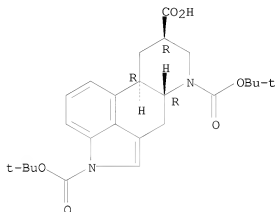
II

AB A process was disclosed for the production of dopamine agonists, such as the

ergoline alkaloid cabergoline (I), and the intermediates thereof. Thus, cabergoline was prepared via a multistep synthetic sequence that started from lysergol and concluded with an amidation reaction with 54.7% yield of acid II with 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride using Et₃N in CH₂Cl₂ at rt for 20 h.

IT 1075250-76-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (process for preparation of cabergoline, a therapeutically useful dopamine agonist and prolactin inhibitor)
 RN 1075250-76-8 CAPLUS
 CN Ergoline-1,6,8-tricarboxylic acid, 1,6-bis(1,1-dimethylethyl) ester, (8β)- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN
 ACCESSION NUMBER: 2005:1004742 CAPLUS
 DOCUMENT NUMBER: 143:286587
 TITLE: Novel process for production of cabergoline
 INVENTOR(S): Galambos, Janos; Czibula, Laszlo; Sebok, Ferenc;
 Balint, Sandorne; Kassai, Ferencne; Ignaczne Szendrei,
 Gyoergyi; Demeter, Adam
 PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085243	A2	20050915	WO 2005-HU22	20050302
WO 2005085243	A3	20060406		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

HU 2004000517	A2	20051128	HU 2004-517	20040304
HU 2004000517	A3	20060529		
EP 1720869	A2	20061115	EP 2005-718154	20050302
EP 1720869	B1	20100526		

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

AT 469149	T	20100615	AT 2005-718154	20050302
IN 2006KN02135	A	20070518	IN 2006-KN2135	20060728
US 20070293677	A1	20071220	US 2007-591202	20070613

PRIORITY APPLN. INFO.: HU 2004-517 A 20040304
 WO 2005-HU22 W 20050302

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
 OTHER SOURCE(S): CASREACT 143:286587; MARPAT 143:286587
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

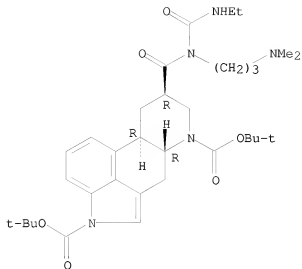
AB A process for preparing cabergoline (I) from
 ergoline-8 β -carboxylic acid ester (II; R= H; R1 = C1-4 alkyl)
 comprises the following steps: (a) reacting an ergoline-8 β -carboxylic
 acid ester II (R = H), in the presence of a catalyst (i) with a compound
 X-COOR2 [R2 = (un)substituted straight or branched C1-6 alkyl, X = Br,
 Cl], or (ii) with a compound O(COOR2)2; (b) reacting the obtained carbamate
 derivative II (R = CO2R2) with 3-(dimethylamino)propylamine (DMAPA) in the
 presence of a catalyst; (c) reacting the obtained
 ergoline-8 β -carboxamide derivative III (R = CO2R2) with Et isocyanate
 (EtNCO) in the presence of ligand(s) and Ib and IIb metal group salt
 catalysts; (d) reacting the obtained protected N-acylurea derivative IV (R =
 CO2R2) with a strong aqueous inorg. acid; (e) reacting the obtained secondary
 amine V with an electrophilic allyl alc. derivative in the presence of a
 palladium or nickel containing catalyst and optionally in the presence of
 ligand(s) to form I. The intermediates of II (R = CO2R2), III (R =
 CO2R2), IV (R = CO2R2) and V are novel. The polymorphic amorphous form of
 I and the production thereof.

IT 864366-98-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and N-dealkoxycarbonylation of; novel process for production of
 cabergoline polymorphs)

RN 864366-98-3 CAPLUS

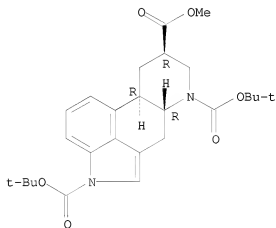
CN Ergoline-1,6-dicarboxylic acid, 8-[[[3-
 (dimethylamino)propyl] [(ethylamino)carbonyl]amino]carbonyl]-,
 bis(1,1-dimethylethyl) ester, (8 β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IT 864447-98-3P, 1,6-Di(tert-butoxycarbonyl)ergoline-8β-carboxylic acid methyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and amidation of, with (dimethylamino)propylamine; novel process for production of cabergoline polymorphs)
 RN 864447-98-3 CAPLUS
 CN Ergoline-1,6,8-tricarboxylic acid, 1,6-bis(1,1-dimethylethyl) 8-methyl ester, (8β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

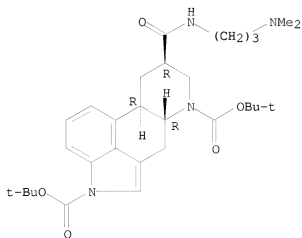


- IT 864366-97-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and carbamylation of, with Et isocyanate; novel process for production of cabergoline polymorphs)
 RN 864366-97-2 CAPLUS
 CN Ergoline-1,6-dicarboxylic acid, 8-[[[3-(dimethylamino)propyl]amino]carbonyl]-, bis(1,1-dimethylethyl) ester,

10/591,202

(8 β)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN

RE CITED REFERENCES

(1) Anon; WO 02085902 A1 CAPLUS

(2) Anon; US 20020177709 A1

(3) Anon; US 5382669 A CAPLUS

=> d his

(FILE 'HOME' ENTERED AT 14:07:20 ON 24 SEP 2010)

FILE 'REGISTRY' ENTERED AT 14:07:36 ON 24 SEP 2010

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 4 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:10:19 ON 24 SEP 2010

L4 3 S L3

L5 735 S CABERGOLINE

L6 3 S L4 AND L5

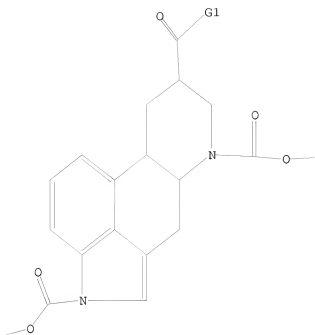
L7 3 S L4 OR L6

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/591,202



G1 O,N

Structure attributes must be viewed using STN Express query preparation.

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